82. POSTER SESSION
Geriatric Infectious Diseases
Saturday, noon - 2 p.m.
Exhibit Hall A

516 A Randomized Controlled Trial of Doxycycline and Rifampin for Patients with Alzheimer Disease

MARK LOEB, MD, WILLIAM MOLLOY, MD, FRCP, MAREK SMIEJA, MD, PhD, TIM STANDISH, CHARLES GOLDSMITH, PhD, JIM MAHONY, PhD, STEPHANIE SMITH, MARTIN O'DONNELL, MD, MAX CHERNESKY, PhD, McMaster Univ., Hamilton, ON, Canada; MICHAEL BORRIE, MD, Univ. of Western Ontario, London, ON, Canada; EARL DECOTEAU, MD, Univ. of Saskatchewan, Saskatoon, SK, Canada; WARREN DAVIDSON, MD, The Moncton Hosp., Moncton, NB, Canada; ALLAN MCDOUGALL, MD, Grey Bruce Medical Ctr., Owen Sound, ON, Canada and JUDY GNARPE, PhD, Univ. of Alberta, Edmonton, AB, Canada

Introduction: Doxycycline and rifampin are active against the bacterium *Chlamydia pneumoniae.* Because of chronic inflammation and detection of *C. pneumoniae* in the brains of Alzheimer Disease (AD) patients, the question of whether *C. pneumoniae* has an etiologic role in AD has been raised. Tetracyclines and rifampin have also been shown *in vitro* to interfere with the accumulation of amyloid beta peptide and subsequent development of beta-amyloid fibrils, essential steps in the pathogenesis of AD. **Objective:** To assess whether doxycycline and rifampin have a therapeutic role in patients with AD. **Methods:** We conducted a randomized, triple-blinded, controlled trial in three tertiary care and two community geriatric clinics in Canada. One hundred and one patients with proable AD and a mild to moderate dementia were randomized to either oral daily doses of doxycycline 200 mg and rifampin 300 mg for three months or to placebo. The primary outcome was a change in Standardized Alzheimer's Disease Assessment Scale congitive subscale (SADAScog) at 6 months. Secondary outcomes were changes in the SADAScog at 12 months, test of dysfunctional behavior, depression, and functional status. **Results:** There was a significant reduction in decline in the SADAScog score at 6 months in the antibiotic group compared to placebo group, (−2.75 points, 95% confidence intervals [CI] −5.28 to −0.22, P=0.034). At 12 months the difference between groups in the SADAScog was −4.31 points, 95% CI - 9.17 to 0.56, P=0.079. The antibiotic group showed a significantly reduced decline in Standardized Mini-Mental Status Exam Scores at 12 months (2.20, 95%CI 0.21 to 4.20, P=0.032) and significantly less deterioration in functional status, depression, and dysfunctional behavior at 3 months. There was no significant difference in adverse events between groups (P=0.34). There were no differences in *C. pneumoniae* detection by PCR or antibodies (IgG or IgA) between groups. **Conclusions:** Therapy with doxycycline and rifampin may have a therapeutic role in patients with mild to moderate AD. The mechansim is unlikely to be due to their effect on *C. pneumoniae.* More research is needed to investigate these agents.

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Infectious Diseases Society of America ■ 66 Canal Center Plaza, Suite 600 ■ Alexandria, VA 22314
Phone: (703) 299-0200 ■ Fax: (703) 299-0204 ■ Email: info@idsociety.org

Introduction: Tuberculosis (TB) is a rare cause of female genital tract infection in the United States (US) but should be suspected in women with infertility, menstrual abnormalities or abdominal or pelvic pain, and a positive tuberculin skin test. **Case report:** Case 1: 65-year-old Italian-born white female had persistent right flank pain for more than one year. A dilatation and curettage yielded no diagnosis. PPD was positive. Endometrial biopsy showed caseating granuloma with positive AFB stain, and culture grew Mycobacterium tuberculosis (MTB) susceptible to all first-line agents. Treatment with isoniazid, rifampin, pyrazinamide, and ethambutol for two months, followed by four months of isoniazid and rifampin achieved a good clinical response. Case 2: A two-month-old infant was evaluated for facial palsy, ear drainage, lethargy and weak cry. Enlarged lymph nodes and splenomegaly were noted on physical exam. Chest x-ray was abnormal. PPD was positive. MTB grew from cultures of the left mastoid, middle ear, and multiple gastric aspirates. The mother, a 31-y-o US-born itinerant white female, was sought for evaluation. She was asymptomatic three weeks after hospital treatment with ciprofloxacin for kidney stone and urinary tract infection.. A positive PPD represented conversion within two years. Chest x-ray showed resolving atelectasis. Endometrial biopsy was consistent with granulomatous endometritis; culture was positive for MTB. Restriction fragment length polymorphism on MTB organisms from mother and infant had matching patterns. Six months of anti-TB treatment was administered. The patient subsequently became pregnant. **Conclusion:** We report two cases of endometrial TB. Although this entity is rare in the US, it should be considered in the differential diagnosis of patients with infertility, pelvic pain, and/or menstrual abnormalities, particularly in older women exposed to TB before the advent of chemoprophylaxis, pregnant or post-partum females known to have been recently infected, and in those who migrated from countries with endemic TB.

414 Extrapulmonary Tuberculosis among Somali Immigrants in Minnesota

R. BRYAN ROCK, MD, Univ. of Minnesota, Minneapolis, MN; WENDY MILLS, MPH, Minnesota Dept. of Health, Minneapolis, MN and DAVID N. WILLIAMS, MD, Hennepin County Medical Ctr., Minneapolis, MN

Objective: To characterize extrapulmonary *Mycobacterium tuberculosis* cases in ethnic Somalis in Minnesota. **Methods:** Identification of all cases of tuberculosis in ethnic Somalis in Minnesota from January 1, 1993 to December 31, 2001 were obtained from data collected by the Minnesota Department of Health. Cases were defined as culture positive or radiographic findings consistent with tuberculosis and clinical improvement with antituberculosis therapy. **Results:** A total of 283 cases of tuberculosis among ethnic Somalis were reported, with 155 (55%) cases of extrapulmonary disease among these. The annual rate of TB for Somalis in Minnesota was 654 per 100,000 and the rate of extrapulmonary TB was 412 per 100,000 in 2001. Fifty-seven percent of patients were female and 43% were male. Eighty-three percent were evenly split among the age ranges of 15-24 years-old and 25-44 years-old. Over 75% of the patients had refugee status. Only 1.8% were positive for HIV. Eighty-two percent were known to be PPD positive and 80.6% were culture confirmed. Just under half (45%) had lymph node involvement. The overall rate of resistance for any drug was 24%, with an INH resistance rate of 19.2% and MDR rate of 3.2%. From 1993 to 2000 treatment was completed in 88% of patients, with 80% of them completing their treatment in less than 12 months. **Conclusions:** Extrapulmonary tuberculosis is as common as pulmonary tuberculosis in Somali immigrants to Minnesota. The patients are characteristically young, have low HIV rates, and are predominately female. Some form of resistance is present a quarter of the time. Health-care providers and civil surgeons need to maintain a high level of suspicion for extrapulmonary tuberculosis in this patient population.

415 Pulmonary Tuberculosis and Coccidioidomycosis Coinfection at a State Tuberculosis Hospital

GUNTHER HSUE, MD, Brooke Army Medical Ctr., Ft. Sam Houston, TX and ROBERT N. LONGFIELD, MD, Texas Ctr. for Infectious Diseases, San Antonio, TX

Pulmonary tuberculosis (TB) and coccidioidomycosis (CM) can present with similar clinical symptoms and chest radiographs, but require different treatment. Historical reviews of small numbers of cases in the 1950-1970's have indicated that coinfection may occur among TB patients living in CM endemic areas. We evaluated coinfection with CM in our TB hospital over the past 8 years. We performed a retrospective, inpatient chart review at a tertiary referral TB hospital between 1995 and 2003, to find TB patients with evidence of concomitant pulmonary CM. Active TB disease case controls were also identified. 8 out of 1219 (0.656 % incidence) inpatients during this 8-year period had positive sputum cultures for both TB and CM. Chest radiograph/CT scan, CM serologies, TB and CM culture reports and patients' clinical course were reviewed. Death occurred in the single HIV-positive TB patient with disseminated CM. 6 out of 8 patients were treated with antifungal agents in addition to their TB medications. 1 patient was transferred to another hospital, 3 were discharged home, and 4 subsequently left against advice. Pulmonary coinfection with TB and CM continues to occur in susceptible populations in CM endemic areas, although very infrequently. Coinfection with CM should be considered in the differential diagnosis of a TB patient on appropriate therapy with either a worsening clinical condition or changing chest radiographs in a CM endemic location.

416 Molecular Analysis of Frozen Sarcoidosis Tissues for the Presence of *Mycobacterium* DNA

WONDER P. DRAKE, MD, LEIGH G. POWERS, BS, TIMOTHY L. COVER, MD, Vanderbilt Univ. Medical Ctr., Nashville, TN and MARTIN BLASER, MD, New York Univ. Medical Ctr., New York, NY

Background: Sarcoidosis is a multisystem granulomatous disease whose etiology is unknown. In a previous study (Drake et al. *Emerg Infect Dis* 2002; 8:1334), we found evidence for the presence of *Mycobacterium* species in 15(60%) of 25 formalin-fixed tissues from patients with sarcoidosis, and from 0/25 controls ($p<0.00002$, chi square). We extended these results by analyzing frozen tissue specimens obtained from patients at different institutions. **Methods:** Frozen specimens from twenty patients (sarcoidosis pulmonary tissues=10, control tissues=10) were studied. Polymerase chain reaction (PCR) assays were performed to detect *Mycobacterium* 16S rRNA, *rpoB*, and IS*6110* sequences. The sensitivity of each PCR assay was 10^0 -10^2 genome copies. All specimens negative for *Mycobacterium* nucleic acids were subsequently subjected to nested PCRs, which possessed sensitivities of one genome copy per assay. **Results:** Five of ten sarcoidosis specimens tested positive for *Mycobacterium* 16S rRNA ($p=0.016$, Fisher's exact test). Four 16S sequences possessed 100% positional identity with *Mycobacterium tuberculosis*, and one contained a single nucleotide polymorphism (A◇G at position 355). None of the sarcoidosis specimens yielded IS*6110* amplicons. Three of the five specimens positive for 16S rRNA also possessed *Mycobacterium rpoB* sequences. The *rpoB* sequences possessed 99% positional identity with *M. tuberculosis,* but all 3 contained two polymorphisms (G◇C at position 2312 and T◇C at position 2313). None of the control tissues were positive for *Mycobacterium* 16S rRNA, *rpoB,* or IS*6110* products. **Conclusions:** We detected *Mycobacterium* 16S rRNA and *rpoB* sequences in five of ten sarcoidosis specimens compared to none of ten control specimens. Based on the detection of the nucleotide polymorphisms in 16S rRNA and *rpoB*, and the absence of IS*6110,* we speculate that a novel variant of *M. tuberculosis* may be present in sarcoidosis lesions.

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